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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,161	03/04/2002	Yuichi Oku	MIT-C205	9188

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EXAMINER	
COUNTS, GARY W	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 04/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/070,161	OKU ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-7,9-23 and 26-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-7,9-23 and 26-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed March 24, 2006 is acknowledged and has been entered.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 4-7, 9-11, 13, 14, 16, 18-23 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Niemeyer et al (US 2003/0118595) in view of Bayer et al (Immunoassay, edited by Diamandis et al, Chapter 11, The Avidin-Biotin System, 1996, pgs 237-267).

Niemeyer et al disclose methods and kits comprising bioconjugates for determining a target analyte of interest. Niemeyer et al disclose a solid phase (chip) having oligonucleotides (R3) immobilized on the solid phase (p. 14, paragraph 0127, lines 1-5). Niemeyer et al disclose a bioconjugate (receptor II) comprising DNA-STV hybrids (DNA (B3)- STV (strepavidin, R2) bound to a biotinylated (B2) antibody (L2) (p. 14, para. 0127, lines 9-10). Niemeyer et al disclose that the solid phase oligonucleotides (R3) is capable of binding to the DNA (B3) of the DNA-STV hybrid. Niemeyer et al disclose that the bioconjugate binds to a target analyte such as an antibody (p. 14, para. 0127, lines 11-13). Niemeyer et al disclose that the target can be detected by another receptor (secondary antibody conjugate (L1-M))(see Fig. 5, para. 0127, lines 14 & 15, see also attachment B which was provided by Applicant in the response filed 03/06/06).

Niemeyer et al differ from the instant invention in failing to specifically teach receptor I is L1-B1-R1-M. Niemeyer et al also differs from the instant invention in failing to specifically teach R1 or R2 has a plurality of binding points with respect to B1 or B2, and a plurality of ligands L1 or L2 are bound to the R1 substances and the substance B1 (as recited in claims 4-7). Niemeyer et al also differs from the instant invention in

failing to specifically teach the solid phase conjugate is stored within the kit separate from at least receptor II.

Bayer et al disclose receptors which can be used in immunoassays. Bayer et al disclose that the receptors are complexes which are used in immunoassays to detect an analyte of interest (p. 251-254). Bayer et al disclose the receptor I can be comprised of antibody (L1), biotin (B1), avidin (R1) and enzyme (M). Bayer et al also disclose that avidin (interchangeable with strepavidin, p. 238) occurs in solution as a tetramer and thus has four binding biotin-binding sites per molecule (238). Bayer et al disclose that a plurality of biotinylated probes such as biotinylated (B1 or B2) antibodies (L1 or L2) can be bound to avidin R1 or R2) (p.251-252). Bayer et al disclose this provides for improved detection systems and improved sensitivity and provides for a very efficient alternative to the sequential approach because the preformed complexes save one of the steps in the immunoassay and second, the signal is often higher due to the multiplicity of probe molecules contained in the complex.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute receptor complexes as taught by Bayer et al for the detection receptor of Niemeyer et al because Bayer et al shows that this provides for improved detection systems and improved sensitivity and provides for a very efficient alternative to the sequential approach because the preformed complexes save one of the steps in the immunoassay and second, the signal is often higher due to the multiplicity of probe molecules contained in the complex. Thus, one of ordinary skill in

the art would have a reasonable expectation of success incorporating receptor complexes as taught by Bayer et al into the method of Niemeyer et al.

It would have also been obvious to one of ordinary skill in the art to incorporate a plurality of biotinylated antibodies such as taught by Bayer et al into the method and kit of Niemeyer et al specifically teaches the use of avidin-biotin systems and Bayer et al teach these systems provide for the introduction of preformed complexes and that the signals achieved using complexes are often superior to those achieved using conjugates.

Niemeyer et al and Bayer et al disclose the claimed invention except for the solid phase conjugate separate from the receptor II (as recited in claim 1). It would have been obvious to one having ordinary skill in the art at the time the invention was made to form the solid phase conjugate and receptor II as separate components and place them into the kit separately, since it has been held that constructing a formerly integral structure in various elements involves only routine skill in the art. *Nerwin v. Erlichman,* 168 USPQ 177, 179.

With respect to claims 5 and 7 as instantly recited since the combination of Niemeyer et al and Bayer et al disclose the same bioconjugates as recited in the claims the bioconjuates of Niemeyer et al and Bayer et al would appear to have plural types of reactivity. Further, Niemeyer et al disclose that the ligand can be a polyclonal antibody (p. 7) which binds to different epitopes on an antigen.

With respect to claim 13 since the combination of Niemeyer et al and Bayer et al disclose the same substances B1, R1, B2 and R2 as applicant. It is inherent that the dissociation constant be from 10^{-8} to 10^{-16}.

With respect to claim 19 since Bayer et al teaches that avidin and streptavidin are interchangeable and are actually different molecules. It would have been obvious to one of ordinary skill in the art to replace one with the other in one of the receptor molecules because it is known in the art that avidin is an alternative for strepavidin and vice versa.

With respect to claim 28 the combination of Niemeyer et al and Bayer et al disclose that the receptor I and receptor II are different reagents and used in a sequential manner and thus one of ordinary skill in the art would recognize that the reagents are separate within the modified kit of Niemeyer et al.

5. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Niemeyer et al and Bayer et al in view of Ghosh et al (US 5,237,016).

See above for the teachings of Niemeyer et al and Bayer et al.

Niemeyer et al and Bayer et al differ from the instant invention in failing to specifically teach the analyte A is DNA and the ligands L1 and L2 are complementary to different portions of the analyte A.

Ghosh et al disclose the detection of nucleic acid such as DNA. Ghosh et al disclose the use of oligonucleotide probes (ligands) to detect the nucleic acid. Ghosh et al disclose that the first oligonucleotide is complementary to at least a region of the

nucleic acid and that the second oligonucleotide is complementary to a different region of the nucleic acid (col 1- col 2).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate oligonucleotides into the modified method of Niemeyer et al because Niemeyer et al specifically teaches that nucleic acids can be the target and is generic with respect to the reagents to be used in this assay. Further, Niemeyer et al is generic with respect to the nucleic acid that is to be detected and one would use the appropriate reagent, i.e. oligonucleotides to detect the desired analyte, in this case DNA.

6. Claims 15 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Niemeyer et al and Bayer et al in view of Billing-Medel et al (US 2002/0142371).

See above for the teachings of Niemeyer et al and Bayer et al.

Niemeyer et al and Bayer et al differ from the instant invention in failing to specifically teach that the B1 and/or the substance B2 and wherein the substance R1 and/or the substance R2 is selected from the group consisting of DNA, RNA, antigen, antibody, lection, glycoprotein and sugars.

Billing-Medel teach assays in which specific binding members are used. Billing Medel teaches that specific binding member is a member of a specific binding pair. That is two different molecules where one of the molecules, through chemical or physical means, specifically binds to the second molecule. Billing-Medel teaches that antigen and antibody specific binding pairs are common in immunoassays and that other specific binding pairs include biotin and avidin, and carbohydrates and lectins.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate antigen/antibody pairs as taught by Billing-Medel et al into the modified method of Niemeyer et al because Billing-Medel et al teaches that the use of antigen/antibody pairs are known in the art. Therefore, one of ordinary skill in the art would have a reasonable expectation of success incorporating antigen/antibody pairs as taught by Billing-Medel et al into the method and kit of Niemeyer et al.

7. Claims 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Niemeyer et al and Bayer et al in view of Millipore (A Short Guide to Developing Immunochromatographic Test strips, pp. 1-36, Nov. 1996).

See above for the teachings of Niemeyer et al and Bayer et al.

Niemeyer et al and Bayer et al differs from the instant invention in failing to teach the marker is detected as a line.

Millipore disclose nitrocellulose membranes (same as taught by Niemyer et al) as solid supports used in assays. Millipore teaches that the reagents used to capture a target are immobilized into the formation of a line on the membrane and that formation of a line caused by detection reagents capture within this region indicates the presence of the target.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate a solid phase system as taught by Millipore with the modified method and reagents of Niemeyer et al because Niemeyer et al specifically teaches that their methods can use nitrocellulose supports and visual detection reagents and Millipore shows that the formation of a colored line is well known in the art

of assays. Therefore one of ordinary skill in the art would have a reasonable expectation of success incorporating a solid phase system comprising capture reagents immobilized in the formation of a line with the method and reagents of Niemeyer et al.

Response to Arguments

8. Applicant's arguments, see amedment, filed March 24, 2006 have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made. See above for the rejections

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary Counts
Examiner
Art Unit 1641
April 3, 2006

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04/04/06